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More severe course of delta hepatitis in HIV-infected patients [L]

HIV infection alters the course of both hepatitis B and C virus infections, increasing carriage states and viral replication.^{1,2} Interestingly, the effect is the opposite in terms of liver disease. Milder liver injury is seen in patients with chronic hepatitis B who become severely immunosuppressed, despite extremely high levels of HBV viraemia.¹ In contrast, rapidly progressive liver disease seems to occur in HIV-infected patients with chronic hepatitis C³; while HCV viremia rises as the CD4 + T cell count falls.²

In regions such as Spain, where drug addicts make up a large part of the HIV-positive population, delta hepatitis is the main cause of severe liver disease in HIV-infected patients.⁴⁻⁶ However, little is known on the effect of the interaction of HIV and hepatitis delta virus (HDV). Since HIV infection may be an important predisposing factor for premature liver cirrhosis in patients with chronic hepatitis D, we analysed the features of 27 HIV-positive patients suffering chronic delta hepatitis and compared them with those from 10 patients with chronic hepatitis D without HIV infection.

We reviewed the clinical charts of 37 patients attending our institution from 1989 to 1993, fulfilling the criteria for chronic hepatitis D (persistent hypertransaminaemia, positive HBsAg in sera, and presence of delta antibody). As shown in the table, gender and age were similar in both HIV-positive and -negative individuals. However, previous or current drug addiction practices were admitted by 96% of the former and only by 30% of

the latter. Probably for this reason HCV coinfection was also more prevalent in the HIV-positive than in the HIV-negative population (85% vs 20%). Mean alanine aminotransferase levels were higher (twice) in subjects with HIV infection than in those HIV-negative, and previous episodes of hepatic decompensation (ascites, encephalopathy, and/or jaundice) were recognised more often in the former. Indirect signs of portal hypertension (as manifested at physical examination, ultrasonography and gastroduodenal endoscopy) also tended to be more frequent in HIV infected patients with chronic hepatitis D than in HIV-negatives. Liver biopsy had been performed in 13 patients (8 HIV-positive and 5 HIV-negative), and histological findings were not significantly different comparing the groups, as chronic active hepatitis with cirrhosis was the most common diagnosis.

The reasons for this apparent more severe course of chronic hepatitis D in HIV-infected patients were investigated. We found a higher level of HDV replication in them, as reflected by the recognition of circulating delta antigen in a quarter of HIV-positives but only in one out of 10 HIV-negative patients. Interestingly, HBV replication which usually is suppressed in HDV superinfection, remained elevated in these HIV-immunodeficient patients (mean CD4 + T cell count was 172, SD 86 per mm³): serum HBeAg was detected in nearly half of the HIV-infected patients and in none of those HIV-negative, and HBV-DNA was positive in two thirds of the former and in none of the latter. In seven cases, delta antigenaemia coexisted with detectable HBeAg in sera, and all these patients showed very high aminotransferase levels.

In immunocompetent individuals, the presence of multiple hepatitis virus infections seems to favour the predominant replication of one virus instead of the others.⁷ We recently demonstrated that in HIV-positive patients with severe immunodeficiency, this reciprocal inhibitory effect seems to be lost.⁸ Thus, high replicative kinetics are recognised for all coincident hepatitis viruses. Since impaired cellular immune function does not affect chronic HDV or HCV liver injury, as characteristically is seen for chronic hepatitis B, the direct cytopathic effect of these viruses could be enhanced with higher levels of HDV and HCV replication, leading to rapidly progressive liver disease.

In conclusion, we found a more severe

Characteristic findings of chronic hepatitis D in a cohort of HIV-positive and HIV-negative individuals

| Variables | HIV+ (n = 27) | HIV- (n = 10) | p |
|---------------------------|------------------|------------------|-------|
| Gender (male:female) | 25:2 | 9:1 | NS |
| Mean age (years) | 32 (20-46) | 25 (19-38) | NS |
| Parenteral drug addiction | 26 (96%) | 3 (30%) | <0.01 |
| Mean ALT levels | 175 | 79 | <0.05 |
| Hepatic decompensation | 10 (37%) | 1 (10%) | <0.01 |
| Portal hypertension | 16 (59%) | 4 (40%) | NS |
| Circulating delta antigen | 7 (26%) | 1 (10%) | <0.05 |
| Positive serum HBeAg | 11 (41%) | 0 | <0.01 |
| Positive anti-HCV | 23 (85%) | 2 (20%) | <0.01 |

course of chronic hepatitis D in our cohort of HIV-immunosuppressed patients, and we postulate that high replication of the delta virus and the presence of HCV co-infection, in conjunction, could explain this worse outcome.

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Spontaneous loss of PPNG resistance plasmids

The Scottish *Neisseria gonorrhoeae* Reference Laboratory Annual Report for 1992¹ highlighted one of the points made in the study on gonococcal epidemiological data² from Stockholm, Sweden.

A small cluster of penicillinase-producing *Neisseria gonorrhoeae* (PPNG) infection in Central Region, Scotland, demonstrated spontaneous loss of plasmid encoding during the process of clinical assessment, screening and treatment. Patient 1 who attended on 17 August 1992 with minor vulvodynia (and who had had a hysterectomy in 1986) was found to have a gonococcal infection with a PPNG isolate of serovar IB-1/Bopst. Her partner, who was contact traced on 2 September 1992 and reported a casual contact in Tenerife, was also shown to be infected with a IB-1/Bopst PPNG isolate. It is of interest that the casual contact originated from a Scottish Health Board Area (Fife) adjacent to Central Region. Patient 3 (no connection with nos 1 & 2) attended with urinary symptoms on 10 September 1992 with positive microscopy and a IB-1/Bopst non-PPNG isolate was reported. His partner was contact traced on 11

September 1992, had complained of cystitis over a five month period, and a IB-1/Bopst PPNG (showing a weak reaction in the chromogenic cephalosporin test) was isolated; the culture was later shown to contain both penicillin sensitive and penicillin resistant IB-1 isolates. A repeat culture from the same patient received one week later was found to be IB-1/Bopst non-PPNG. All of the PPNG isolates carried 2.6, 3.05 and 24.5 MDa plasmids, were non-requiring (NR) on auxotyping and had a ciprofloxacin MIC of 0.06 mg/l. The non-penicillinase isolates were also auxotype NR with a ciprofloxacin MIC of 0.06 mg/l. There were no other IB-1/Bopst strains isolated in Scotland during 1992.

As all patients were contact traced, the cluster of infection was contained with the added bonus of demonstrable spontaneous loss of β -lactamase plasmid during surveillance. This report also highlights the importance of national surveillance. It is unlikely that the probable source of infection in Tenerife, who originated from Fife, has returned to Scotland with an infection as this would have been detected through the Scottish *Neisseria gonorrhoeae* Reference Laboratory.

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Disseminated infection due to penicillin resistant gonococci—is it still rare?

Penicillin resistant gonococci have only rarely been implicated in disseminated gonococcal infection. Two reports attributed two separate cases of gonococcal arthritis to penicillinase producing organisms but these cases were not well documented.^{1,2} In neither case was the organism cultured directly from a disseminated site and the relation of the arthritis to the gonococcal infection was presumptive, being based on positive throat or urethral cultures. However, five cases of gonococcal arthritis due to penicillinase producing organisms that were cultured directly from infected joints have been reported.³ As an addition to these cases, we describe a case of gonococcal arthritis due to penicillinase producing organisms, based on culture from the infected joint.

A 25 year old West Indian woman was admitted to the orthopaedic department in September 1993 with a history that following return from Jamaica, she was suffering from flitting joint pain affecting particularly her